## FACT SHEET
### HBM value for DPHP

**Substance name**  Di-2-propylheptylphthalate; 1,2-Benzenedicarboxylic acid bis(2-propylheptyl) ester

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value / Descriptor</th>
<th>Dimension</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HBM Guide value</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Guide value I (HBM-I, precautionary value)</strong></td>
<td>Children: 1 Adults: 1,5</td>
<td>mg/L</td>
<td>Morning urine/spot urine (rounded value)</td>
</tr>
<tr>
<td>Year of issue</td>
<td>2014</td>
<td></td>
<td></td>
</tr>
<tr>
<td>status</td>
<td>final</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### General Information

**CAS No**  53306-54-0

**IUPAC name**  Bis(2-propylheptyl) phthalate

**Molar mass substance**  446.7 g/mol

**HBM-parameter**  oxidized monoester oxo- MPHP and OH-MPHP specific metabolites, limit of quantification: 0.25 – 0.30 µg/L [1]

**Molar mass metabolites**  320.4 and 322.4; mean: 321.4 g/mol

### Database

**Tolerable intake**  (TDI, RfD or comparable)

RfD: 0.1 mg/(kg KG · d), based on human equivalent BMDL₀ for effects on thyroid gland (Bath et al., 2014) [2]; value given for further information, not used as POD by the HBM commission

**Key study / Author(s) (Year)**  BASF (1995a) selected as key study by the HBM Commission

**Species**  Wistar rats

**Route/type of study**  oral/ subchronic OECD 408

**Study length (Exposure duration)**  3 month

**Exposure pattern**  with feed

**Critical endpoint/ effect**  effects on thyroid gland and pituitary gland (BfR 2011) [3]

**POD<sub>HBM-I</sub>**  40 mg/(kg bw · d) NOAEL

### Assessment factors

**Dose-response assessment factor**  n.a.

**Severity of effect**  -

**Adjusted exposure duration factor (time scaling)**  n. a. Oral study

**Adjusted study length factor**  2 Subchronic → chronic
### Route-to-route extrapolation factor
- n. a.

### Adjusted absorption factor
- n. a.

### Interspecies factor
- 10

### Intraspecies factor
- 10

### Sensitive population factor
- 1

### Other adjustment factors
- Quality of whole database: -

### Total assessment factor (TAF)
- 200

### Kinetic terms

<table>
<thead>
<tr>
<th>Term</th>
<th>Description</th>
<th>Calculation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor for metabolic conversion (Fue)</td>
<td>0.24 [4]</td>
<td>48h, oxo-MPHP and OH-MPHP</td>
</tr>
<tr>
<td>Proportion molar mass metabolites to molar mass DPHP</td>
<td>0.72</td>
<td>321.4 / 446.7</td>
</tr>
</tbody>
</table>

### Urine volume
- Children: 0.03 L/(kg bw · d)
- Adults: 0.02 L/(kg bw · d)

### Result (Calculation)

<table>
<thead>
<tr>
<th>Term</th>
<th>Description</th>
<th>Calculation</th>
</tr>
</thead>
<tbody>
<tr>
<td>POD_{HBM-I}/TAF (TDI analog)</td>
<td>0.2</td>
<td>mg/(kg bw · d)</td>
</tr>
<tr>
<td>kinetic extrapolation and HBM value calculation [5]</td>
<td>200 x 0.72 x 0.24 = 34.56</td>
<td>µg/(kg bw · d)</td>
</tr>
<tr>
<td></td>
<td>children: 1152 (= HBM-I)</td>
<td>μg/L morning urine</td>
</tr>
<tr>
<td></td>
<td>adults: 1728 (= HBM-I)</td>
<td></td>
</tr>
<tr>
<td>tolerable amount OH-MPHP + oxo-MPHP in the urine = TDI analog x (molecular weight metabolites/molecular weight DPHP) x Fue</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>consideration of urine volume, Children: division by 0.03</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Adults: division by 0.02</td>
<td></td>
</tr>
</tbody>
</table>

### Remarks:
According to the evaluation of the German Bundesinstitut für Risikobewertung (BfR) [3] the technical DPHP consists of approx. 81% Di-2-Propylheptylphthalate, approx. 18% 2-Propylheptylphthalate, 2-Propyl-4-methylhexylphthalate and 1% Di-2-Propyl-4-methylhexylphthalate.

In pursuance of Wittasek and Angerer [6] children seem to have a more effective oxidative metabolism of phthalates compared to adults. Those age specific differences in the human metabolism have not been investigated for DPHP. Likewise no data concerning the correlation between the amount of body burden and the excretion of metabolites exist.

### Rationale

1,2-benzenedicarboxylic acid, di-2-propylheptyl ester (DPHP) is used as plasticizer for the manufacturing of plastics, mainly polyvinylchloride (PVC).

A subchronic feeding study with rats revealed a NOAEL (No Observed Adverse Effect Level) of 40 mg/(kg bw · d), which can be used as point of departure (POD) for the derivation of a HBM-I value. Application of a total assessment factor of 200 leads to an estimation of 200 µg/kg bw as tolerable daily intake of DPHP (TDI analog). On the basis of the results of metabolism studies with humans it is possible to calculate back from the tolerable daily intake of DPHP to the tolerable concentration of specific metabolites in urine. Thus a HBM-I value of 1 mg/L morning urine for children and 1.5 mg/L morning urine for adults was derived for the sum of the oxidized monoesters oxo-MPHP and OH-MPHP, which were identified as robust and conclusive biomarkers for DPHP. Currently available data on concentrations of oxo-MPHP and OH-MPHP in urine samples of the German Environmental Specimen Bank indicate exposure levels clearly below the HBM-I value. Further studies will show if a plateau is already reached or if an increase in the body burden of DPHP and its metabolites will occur as a result of its increasing use as alternative to other phthalates.

The HBM Commission deliberated the HBM value for HBCD on the basis of a dossier prepared by the Fraunhofer Institute (FhG; O. Licht, I. Mangelsdorf and J-U. Voss) on behalf of the Federal Environment Agency.
Literature


